

Fig. 3

SEQ ID NO: 2

MDTSRLGVLL SLPVLLQLAT GGSSPRSGVL LRGCPHCHC EPDGRMLLRV
DCSDLGLSEL PSNLSVFYSY LDLSMNNISQ LLPNPLPSLR FLEELRLAGN
5 ALTYIPKGAF TGLYSLKVLN LQNNQLRHVP TEALQNLRSI QSLRLDANHI
SYVPPSCFSG LHSRLHLWLD DNALTEIPVQ AFRSLSALQA MTLALNKHII
IPDYAFGNLS SLVVLHLHNN RIHSLGKKCF DGLHSLETLD LNYNNLDEFP
TAIRTLNLK ELGFHSNNIR SIPEKAFVGN PSLITIHFYD NPIQFVGRSA
FQHLPELRTL TLNGASQITE FPDLTGTANL ESLTLTGAQI SSLPQTVCNQ
10 LPNLQVLDLS YNLLEDLPSF SVCQKLOKID LRHNEIYEIK VDTFQQLLSL
RSLNLAWNKI AIIHPNAFST LPSLIKLDLS SNLLSSEFPI GLHGLTHLKL
TGNHALQSLI SSENFPKLV IEMPYAYQCC AFGVCENAYK ISNQWNKGDN
SSMDDLHKKD AGMFQAQDER DLEDFLLDFE EDLKALHSVQ CSPSPGPFKP
CEHLLDGWLI RIGVWTIAVL ALTCNALVTS TVFRSPLYIS PIKLLIGVIA
15 AVNMLTGVSS AVLAGVDAFT FGSFARHGAW WENGVGCHVI GFLSIFASES
SVFLLTLAAL ERGFSVKYSA KFETKAPFSS LKVIILLCAL LALTMAAVPL
LGGSKYGASP LCLPLPFGEF STMGYMVALI LLNSLCFLMM TIAYTKLYCN
LDKGDLENIW DCSMVKHIAL LLFTNCILNC PVAFLSFSSL INLTFISPEV
IKFILLVVVP LPACLNPLLY ILFNPHEKED LVSLRKQTYV WTRSKHPSLM
20 SINSDDVEKQ SCDSTQALVT FTSSSITYDL PPSSVPSPAY PVTESCHLSS
VAFVPCL

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Fig. 4 (1/2)

5	LGR5 SEQ ID NO: 2	MDTSRLGVLLSLPVLQLLATGGSSPRSGVLLRGCPHCHCEPDGRMLLRVDCSDLGLSELPSNLSVFTSYLDLSMNNISQ
	LGR6 SEQ ID NO: 3	-----MRLEGEGRSARAGQNLSRAGSARRGAPR-----DLSMNNLTE
	LGR4 SEQ ID NO: 4	-----MPGFLGLLCFLALGLLGSAGPSGAAPFLCAAPCSCDGDRR-----VDCSGKGLTAVPEGLSAFTQALDISMNNITQ
	Consensus/80%b.L.h.Gpts.tG.....sss.pps.sc.....DLSMNNI*p
10	LGR5	LLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVLMLQNNQLRHVPTEALQNLRLSLQSLRLDANHISYVPPSCFSG
	LGR6	LQPLGFHHLRFLEELRLSGNHLSHIPGQAFSGLYSLKILMLQNNQLGGIPAEALWELPSLQSL-----
	LGR4	LPEDAFKNFPFLEELQLAGNDLSFIHPKALSGELKVLTLQNNQLKTVPSEAIRGLHALQSLRLDANHITSVPEDSFEG
	Consensus/80%	L..s.b.pb.FLEELpLtGN.L*aI...Ab*GLbpLKlLhLQNNQL.hLPsEAlb.L.tLQSL.....
15	LGR5	LHSLRHLWLDNALTEIPVQAFRSLALQAMTLALNKIHHIPDYAFGNLSSLVVLHLHNNRIHSLGKKCFDGLHSLETLD
	LGR6	-----D
	LGR4	LVQLRHLWLDNSLTEVPVHPLSNLPTLQALTALNKISSIPDEAFNLSSLVVLHLHNNKIRSLSQHCFDGLDNLETLD
	Consensus/80%D
20	LGR5	LNYNLDEFPTAIRTLNLKELGFHNSNNIRSIPEKAFVGNPSLITIHFYDNPIQFVGRSAFQHLPELRTLTNGASQITE
	LGR6	LNYNKLQEFFVAIRTLGRLOELGFHNNNIKAIPEKAEMGNPLLOTIHFYDNPIQFVGRSAFQYLPKLHTLSLNGAMDIQE
	LGR4	LNYNLGEFFQAIKALPSLKEELGFHNSNISVIPDGAFDGNPLLRTHLYDNPLSFVGNLSDHSLVIRGASMVQQ
	Consensus/80%	LNYNpL.EFF.AI+sLspLpELGFHsNsIpsIP-.AF.GNP.LbTIHbYDNPLpFVGpSAFp.LscL+*LslpGA..lpp
25	LGR5	FPDLTGATANLESLLTGAQISSLPQTVCNQLPNLQVLDLSYNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLSL
	LGR6	FPDLKGTTSLEILTTLTRAGIRLLPSGMCQQLPRLRVLELSHNQIEELPSLHRCQKLEELGLQHNRIWEIGADTFSQLSSL
	LGR4	FPNLTGTVHLESLLTGTKISSIPNNLCQEQMLRTLDSYNNIRDLSFNGCHALEEISLQRNQIYQIKEGTFQGLISL
	Consensus/80%	FpsLpGTspLE.LTLT.s.Ip.lPpshCpbb..LpsL-LSaN.lc-LPSbp.Cp.LpcIsLp+NpIapI..sTFp.L.SL
30	LGR5	RSNLAWNKIAIHPNAFSTLPSLIKLDLSSNLLSSFPITGLHGLTHLKLGTGNHALQSLISSENFPELKVIEPFIYAYQCC
	LGR6	QALDLSWNAIRSIHPEAFSTLHSLVKLDLTDNQLTTLPLAGLGGLMHLKLKGNLALSQAFSKDSFPKLRILEVPFIYAYQCC
	LGR4	RILDLSRNLIHEIHSRAFATLGPITNLDVSENELTSFPTGELNGLNQLKLVGNFKLKEALAAKDFVNLRSLSVPFIYAYQCC
	Consensus/80%	p.LsLtbN.I..IHspAftTL.s.lhpLdI*.NbL**bPh.GL.GL.pLKL.GNb.Lpphbt.csFspL+.lphFYAYQCC
35	LGR5	AFGVCENAYKISNQWNGDNS SMDD-LHKKDAGMFAQDE----RDLEDFLDFEEDLKALHSVQCSFSPGPFKPCHELL
	LGR6	PYGMCAFFKASQWEAEDLHLDDEESSKREPLGLLARQAENHYDQDLDELQLEMEDS-KPHPSVQCSPTPGPEKPCYEYLF
	LGR4	AFWGCDSYANLN----TEDNSLQDHSVAQEKGKCMSTADA-----ANVTSTLENEEHSQIIHCTPSTGAFKPCYEYLL
	Consensus/80%	sahhC.shhphs.....D.p..Dc...pc.h.hb...s.....ph..pbEpp.+sb..lpC*P*sGsFKPCEaLb
40	LGR5	DGWLIRIGVWTIAVLALTCNALVTSTVFR-SPLYISPIKLLIGVIAAVNMLTGVSSAVLAGVDAFTFGSEARHGAWWENG
	LGR6	ESWGIRLAVVAIVLLSVLCNGLVLLTVFAGGPVPLPPVKFVVGAAGANTLTGISCGLLASVDALTFGQFSEYGARWETG
	LGR4	GSWMIRLTVWFIFLVALEFNLLVILTTFE-SCTSLPSSKLFIGLISVSNLFMGIYTGILTFDAVSWGREAEFGIWWETG
	Consensus/80%	.tWhIRlsvWhIh1t1hNhLvh.TsF..tsh.lss.Kbh1GhItssNhbhGl.stlLs.lDAh*aGpFtcaGhbWESG

continued as Fig. 4 (2/2)

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Fig. 4 (2/2)

continued from Fig. 4 (1/2)

5

LGR5 VGCHVIGFLSIFASESSVFLTLAALERGFSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLP
LGR6 LGCRATGFLAVLGSEASVLLTLAAVQCSVSVSCVRAYGKSPSLGSVRAGVLGCLALAGLAAALPLASVGEYGASPLCLP
LGR4 SGCKVAGFLAVFSSESAIFLLMLATVERSLSAKDIMKNGKSNHLKQFRVAALLAFLGATVAGCFPLEHRGEYSASPLCLP
Consensus/80% .GC+shGFLt1btSett1bLLhLAslpptHSp.....pps.b.ph+shhLhshhhAhhtshPLh..toYtASPLCLP

10

LGR5 --LPFGEPSTMGYMVALILLNSLCFLMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNCPVAFLSFSSLIN
LGR6 YAPPEGQPAALGFTVALVMNSFCFLVAGAYIKLYCDLPRGDFEAVWDCAMVRHVAVLIADGLLYCFVAFLSFASMLG
LGR4 --FPTGETPSLGFTVTLVLLNSLAFLMAVIYTKLYCNLEKEDLSENSQSSMIKHVAVLIFTNCIEFCFVAFFSFAPLIT
Consensus/80% ...P.Gpss sbGahVsLlbbNSbsFLhshhhYhKLYCsL.+Dbp...pstMl+HlAbLlFssslb.CPVAfbSftsbls

15

LGR5 LTFISPEVIKFILLVVVPLPACLNPLLYILFNPHEKEDLVSLRKQTYVWTRSKHPSLMSINSDDVEKQSCDS-----TQ
LGR6 LEFVTPEAVKSVLLVVLPLPACLNPLLYLLFNPHERDDLRLRLPR-----AGDSGPLAYAAAGELEKSSCDS-----TQ
LGR4 AISISPEIMKSVTLIFFPLPACLNPFVLYVFFNPKEKEDWKLLKRRVTKKSGSVSVSISSQGGCLEQDFYDCGMYSHLQG
Consensus/80% hh.1*PEhhK.lhLlhhPLPACLNPLLYlbFNP+F+-Db..L+.p.....t.pssl...sts..pc..hDs.....p.

20

LGR5 ALVTFSSSITYDLPPS-----SVSPAYFVTESCHLS-----
LGR6 ALVAFSDVDLILEASEAGRPFGLTYGFPSVTLISCQQPGAPRLEGSHCVEPEGNHFGNPQPSMDGELLRLRAEGSTPAGG
LGR4 NLTVCDCCESFLLTKFVSCKHLIKSHSCPALAVASCQRPEGYWSDCGTQSAHSDYADEEDSFVSDSSDQVQACGRACFYQ
Consensus/80% sLshsssp.hb.h.s.....Ss.pP.h...ssp.s.....

25

LGR5 -----SVAFVPCL
LGR6 GLSGGGGFQPSGLAFASHV
LGR4 SRGFPLVRYAYNLPRVKD-
Consensus/80%slsbs.p.

30